

CLAIMS

What is claimed is:

1. A method of identifying a compound useful for the treatment or prevention of neuropathic pain, comprising:
  - (a) contacting a cell expressing P2X<sub>4</sub> receptor on the surface thereof, with a test compound, in the presence of P2X<sub>4</sub> receptor agonist,
  - (b) determining whether or not said test compound inhibits an interaction of said P2X<sub>4</sub> receptor agonist and P2X<sub>4</sub> receptor on the surface of the cell, and
  - (c) identifying the test compound which inhibits said interaction, as useful for the treatment or prevention of neuropathic pain.
2. The method according to claim 1, wherein the neuropathic pain is tactile allodynia induced after nerve injury.
3. The method according to claim 1, wherein the cell is mammalian cell.
4. The method according to claim 1, wherein the cell does not express any P2X receptors other than P2X<sub>4</sub> receptor.
5. The method according to claim 1, wherein the P2X<sub>4</sub> receptor agonist is ATP or ADP.
6. The method according to claim 1, wherein the contacting step (a) comprises incubating the cell and the test compound in the absence of the P2X<sub>4</sub> receptor agonist, and then incubating them in the presence of the P2X<sub>4</sub> receptor agonist.
7. The method according to claim 1, wherein the determining step (b) comprises measuring P2X<sub>4</sub> receptor-mediated ion flux of at least one ion selected from the group consisting of Na<sup>+</sup>, K<sup>+</sup>, and Ca<sup>2+</sup>.
8. The method according to claim 7, wherein the contacting step (a) is carried out in the presence of the ion.

9. The method according to claim 1, wherein the determining step (b) comprises comparing intensity of the interaction with that of control sample obtained in the absence of any test compounds.
10. A method of identifying a compound useful for the treatment or prevention of neuropathic pain, comprising:
  - (a) contacting a microglia in inactive-form with a test compound, in the presence of microglia-activator,
  - (b) determining whether or not said test compound inhibits an activation of said microglia, and
  - (c) identifying the test compound which inhibits said activation, as useful for the treatment or prevention of neuropathic pain.
11. The method according to claim 10, wherein the neuropathic pain is tactile allodynia induced after nerve injury.
12. The method according to claim 10, wherein the microglia-activator is ATP or ADP.
13. The method according to claim 10, wherein the contacting step (a) comprises incubating the cell and the test compound in the absence of the microglia-activator, and then incubating them in the presence of the microglia-activator.
14. A pharmaceutical composition comprising a P2X<sub>4</sub> receptor inhibitor and a pharmaceutically acceptable carrier.
15. The pharmaceutical composition according to claim 14 for use in treatment or prevention of neuropathic pain.
16. The pharmaceutical composition according to claim 15, wherein the neuropathic pain is tactile allodynia induced after nerve injury.
17. The pharmaceutical composition according to claim 14, wherein the P2X<sub>4</sub> receptor inhibitor is a P2X<sub>4</sub> receptor antagonist.

18. The pharmaceutical composition according to claim 14, wherein the P2X<sub>4</sub> receptor inhibitor is an antibody or an antibody fragment which binds to P2X<sub>4</sub> receptor protein on the cell surface and prevents the interaction between the receptor and its agonist.
19. The pharmaceutical composition according to claim 14, wherein the P2X<sub>4</sub> receptor inhibitor is an antisense nucleic acid molecule that specifically suppresses expression of P2X<sub>4</sub> receptor gene.
20. The pharmaceutical composition according to claim 14, wherein the P2X<sub>4</sub> receptor inhibitor is an siRNA nucleic acid molecule that specifically suppresses expression of P2X<sub>4</sub> receptor gene.
21. The pharmaceutical composition according to claim 14, wherein the P2X<sub>4</sub> receptor inhibitor is a vector expressing an siRNA nucleic acid molecule that specifically suppresses expression of P2X<sub>4</sub> receptor gene.
22. A pharmaceutical composition comprising a microglial activation-inhibitor and a pharmaceutically acceptable carrier.
23. The pharmaceutical composition according to claim 22 for use in treatment or prevention of neuropathic pain.
24. The pharmaceutical composition according to claim 23, wherein the neuropathic pain is tactile allodynia induced after nerve injury.
25. The pharmaceutical composition according to claim 22, wherein the microglial activation-inhibitor is a P2Y<sub>12</sub> receptor inhibitor.
26. A method for treating or preventing neuropathic pain comprising administering to a subject a therapeutically effective amount of P2X<sub>4</sub> receptor inhibitor.
27. The method according to claim 26, wherein the neuropathic pain is tactile allodynia induced after nerve injury.

28. The method according to claim 26, wherein the P2X<sub>4</sub> receptor inhibitor is a P2X<sub>4</sub> receptor antagonist.

29. The method according to claim 26, wherein the P2X<sub>4</sub> receptor inhibitor is an antibody or an antibody fragment which binds to P2X<sub>4</sub> receptor protein on the cell surface and prevents the interaction between the receptor and its agonist.

30. The method according to claim 26, wherein the P2X<sub>4</sub> receptor inhibitor is an antisense nucleic acid molecule that specifically suppresses expression of P2X<sub>4</sub> receptor gene.

31. The method according to claim 26, wherein the P2X<sub>4</sub> receptor inhibitor is an siRNA nucleic acid molecule that specifically suppresses expression of P2X<sub>4</sub> receptor gene.

32. The method according to claim 26, wherein the P2X<sub>4</sub> receptor inhibitor is a vector expressing an siRNA nucleic acid molecule that specifically suppresses expression of P2X<sub>4</sub> receptor gene.

33. The method according to claim 26, wherein the P2X<sub>4</sub> receptor inhibitor is administered intraspinally.

34. The method according to claim 33, wherein the P2X<sub>4</sub> receptor inhibitor is administered by intrathecal injection.

35. The method according to claim 26, wherein the P2X<sub>4</sub> receptor inhibitor is administered in admixture with a pharmaceutically acceptable carrier.

36. A method for treating or preventing neuropathic pain comprising administering to a subject a therapeutically effective amount of microglial activation-inhibitor.

37. The method according to claim 36, wherein the neuropathic pain

is tactile allodynia induced after nerve injury.

38. The method according to claim 36, wherein the microglial activation-inhibitor is a P2Y<sub>12</sub> receptor inhibitor.

39. The method according to claim 36, wherein the microglial activation-inhibitor is administered intraspinally.

40. The method according to claim 39, wherein the microglial activation-inhibitor is administered by intrathecal injection.

41. The method according to claim 36, wherein the microglial activation-inhibitor is administered in admixture with a pharmaceutically acceptable carrier.